

***In Vitro* Cell-Mediated Biomineralization Of 3D Porous Titanium Scaffolds – A Novel Biomimicry Strategy Towards Osteoinductive Carriers**

Arial 12pt, Capitalized first letters for each word

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Arial 11pt, Initials for first name followed by last name, superscript numbers for affiliations, presenting author underlined and corresponding author should be mentioned with “”. Maximum number of authors is 10.*

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In vitro cell-derived mineralized matrix deposition on scaffolds have been shown to induce *in vitro* osteogenic differentiation of progenitor cells, but *in vivo* osteoinductivity of these constructs is so far not apparent. In this study, we have developed three types of biomineralization media (BM) and studied their effect on the osteogenic differentiation and mineralized matrix deposition onto 3D open porous Ti6Al4V scaffolds by human osteoprogenitor cells (hPDCs). In a medium-dependent manner, the three BM enhanced hPDC 3D proliferation and upregulated early (Runx2) and late osteogenic differentiation (Dlx5, Osterix and osteocalcin) markers, as well as BMP2, a Wnt signaling target gene (LEF1) and vascular endothelial growth factor (VEGF) gene expression. Interestingly, the RankL/OPG ratio was also upregulated, which may indicate hPDC modulation in osteoclastogenesis and thus potential for mineralized matrix remodeling. Indeed, principle component analysis showed that the BM treatments resulted in the enrichment of distinct cell populations represented by highly upregulated specific gene clusters. By devitalization mineralized carriers were produced and used as customized delivery vehicle to implant freshly seeded hPDCs in a nude mouse ectopic bone formation model. Encouragingly, all cell-carrier combinations resulted either in bone ossicles containing bone marrow within the scaffold pores or bone formed directly on the scaffold surface. In conclusion, we have presented a novel biomimetic strategy to functionalize 3D porous scaffolds with a cell-derived mineralized matrix in a customized way that can assist the translation to effective bone defect repair.

Arial 11pt, Maximum 1500 characters excluding spaces.